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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,661	09/23/2003	Jean-Claude Yvin	16721-0250 (42528-292745)	1057

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EXAMINER	
HENRY, MICHAEL C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 08/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/668,661	YVIN ET AL.	
	Examiner	Art Unit	
	Michael C. Henry	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03/28/06*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The following office action is a responsive to the Amendment filed, 03/28/06.

The amendment filed 03/28/06 affects the application, 10/668,661 as follows:

1. Claims 1-10 have been canceled. New Claims 11-22 have been added. This leaves claims 11-22.

The responsive to applicants' arguments is contained herein below.

Claims 11-22 are pending in the application

Claim Objections

Claim 11 is objected to because of the following informalities: The claim recites the phrase "laminin" which appears to contains a typographical error. It appears that the word "laminin" should be replaced by the word "laminarin". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "a chemotherapeutic antineoplastic treatment for cancer" in claim 11, is a phrase which renders the claim indefinite. More specifically, it is unclear whether this treatment actually treats cancer or how this treatment is related to treating cancer.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The specification, while being enabling for the promote of the regeneration of the cells in the bone marrow and the peripheral blood of a patient which cells undergo an acute reduction due to the effect of the antineoplastic agent, cyclophosphamide, comprising the administration of a composition comprising cyclophosphamide and laminarin, does not reasonably provide enablement for the treatment of cancer in a patient. First, in claim 11, the applicant claims a chemotherapeutic antineoplastic treatment for cancer comprising administration to a patient of an effective amount of an antineoplastic agent, the improvement comprising administration to said patient, in conjunction with the administration of the antineoplastic agent, of laminarin in an amount effective to promote the regeneration of the cells in the bone marrow and the peripheral blood of the patient, which cells undergo an acute reduction due to the effect of the antineoplastic agent. The treatment of said cancer in a subject by administering said composition is not enabled because of the following.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to

consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a method for treating cancer (any cancer) in a patient by administering a combination of an antineoplastic agent and laminarin to said individual. The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claims are deemed very broad since these claims reads on treating any type cancer and cancer is a group of more than 100 diseases wherein each type of cancer differs from the others in numerous ways.

Regarding the *Wands* factor (4) the predictability or unpredictability of the art:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that the recitation encompasses all cancers, which are known to involve several various possible, different, separate and independent pathologies, etiologies, or symptoms. Furthermore, one cannot extrapolate the teaching of the specification to the claims because it is well known that the art of anticancer drug

discovery for cancer therapy is highly unpredictable. For example, Gura (Science, 1997, 278(5340):1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second para). Further, the refractory nature of cancer to drugs is well known in the art. Jain (Sci. Am., 1994, 271:58-65) teaches that tumors resist penetration by drugs (p.58, col 1) and that scientists need to put expanded effort into uncovering the reasons why therapeutic agents that show encouraging promise in the laboratory often turn out to be ineffective in the treatment of common solid tumors (p. 65, col 3). Curti (Crit. Rev. in Oncology/Hematology, 1993, 14:29-39) teaches that solid tumors resist destruction by chemotherapy agents and that although strategies to overcome defense mechanisms of neoplastic cells have been developed and tested in a number of patients, success has been limited and further teaches that it is certainly possible that cancer cells possess many as yet undefined additional molecular mechanisms to defeat chemotherapy treatment strategies and if this is true, designing effective chemotherapeutic regimens for solid tumors may prove a daunting task (para bridging pages 29-30) and concludes that knowledge about the physical barriers to drug delivery in tumors is a work in progress (p. 36, col 2). In addition, Hartwell et al (Science, 1997, 278(5340):1064-1068) teach that an effective chemotherapeutic must selectively kill tumor cells, that most anticancer drugs have been discovered by serendipity and that the molecular alterations that provide selective tumor cell killing are unknown and that even understanding the detailed molecular mechanism by which a drug acts often provides little insight into why the treated

tumor cell dies (para bridging pages 1064-1065) and Jain (cited supra) specifically teaches that systemic treatment typically consists of chemotherapeutic drugs that are toxic to dividing cells (p. 58, col 2, para 2). Furthermore, anti-tumor agents must accomplish several tasks to be effective. They must be delivered into the circulation that supplies the tumor or metastatic promotor producing cells and interact at the proper site of action and must do so at a sufficient concentration and for a sufficient period of time. It is clear, as disclosed above that the specification does not teach how to make or use a formulation with a targeting molecule. Also, the target cell must not have an alternate means of survival despite action at the proper site for the drug. In addition variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful therapy. The formulation may be inactivated in vivo before producing a sufficient effect, for example, by degradation, immunological activation or due to an inherently short half-life of the formulation. In addition, the formulation may not otherwise reach the target because of its inability to penetrate tissues or cells where its activity is to be exerted, may be absorbed by fluids, cells and tissues where the formulation has no effect, circulation into the target area may be insufficient to carry the formulation and a large enough local concentration may not be established. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed methods with a reasonable expectation of success. In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

Therefore, the skilled artisan would view that the treatment of all cancers/diseases as recited in claims 11, by administering the same particular compound herein, is highly *unpredictable*. Thus, the skilled artisan would view that the treatment of all cancers, which comprises administering to said patient a composition herein, is **highly unpredictable**.

In regard to these *Wands* factors, (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary: Moreover, it is noted that the specification merely provides working examples, e.g., a tests (using Balb/c mice") to demonstrate or evaluate the promoting effects of laminarin on the regeneration of all the cells reduced in mice treated with an antineoplastic drug (see page, 8, lin7 to page 12, table IIb). Moreover, the specification does not provide any working examples or disclosure that indicates what cancer(s) or type of cancer (s) that is being treated, much less how said cancer(s) is been treated.

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the broad treatment of all cancers recited in the instant claims. As a result, it is necessary for one of skill to perform an exhaustive search for the embodiments of treating any cancer or all cancers as recited in the instant claims so as to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation*, with no assurance of success.

In conclusion, the treatment of cancer in a subject is not enabled by the instant disclosure. It should be noted that the dependent claims 12-22, are also encompassed by this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Di Luzio et al. in view of Yvin et al. (US 2003/0119780 A1).

In claim 11, applicant claims a chemotherapeutic antineoplastic treatment for cancer comprising administration to a patient of an effective amount of an antineoplastic agent, the improvement comprising administration to said patient, in conjunction with the administration of the antineoplastic agent, of laminarin in an amount effective to promote the regeneration of the cells in the bone marrow and the peripheral blood of the patient, which cells undergo an acute reduction due to the effect of the antineoplastic agent. Claim 12 is drawn to a chemotherapeutic antineoplastic treatment for cancer according to claim 11, wherein the antineoplastic agent is cyclophosphamide. Claims 13 and 14 are drawn to said chemotherapeutic antineoplastic treatment wherein laminarin is administered by specific routes. Claims 15 and 16 are drawn to said chemotherapeutic antineoplastic treatment wherein laminarin is administered

before, simulataneously with or after the antineoplastic agent or the cyclophosphamide. Claims 17-22 are drawn to said chemotherapeutic antineoplastic treatment wherein laminarin is soluble laminarin.

Di Luzio et al. disclose a method comprising the administration of an effective amount of an the antineoplastic agent, cyclophosphamide for the treatment tumors (cancer) in rats (see abstract). Furthermore, Di Luzio et al. disclose a method comprising the administration of an effective amount of an antineoplastic agent (cyclophosphamide) in conjunction (combination) with an effective amount of a β-1,3 glucan (CAS # 9012-72-0) to rats (see abstract). It should be noted that the language pertaining to the promotion of the regeneration of the cells in the bone marrow and the peripheral blood of the patient, is considered an inherent effect of the laminarin and does not appear alter the treatment of cancer by the said combination of laminarin and antineoplastic agent.

The difference between applicant's claimed method and Di Luzio et al.'s method is that Di Luzio et al. do not use the glucan, laminarin.

Yvin et al. disclose a method treating cancer growth (tumor growth) comprising the administration of an effective amount of soluble laminarin to mice (see page 4, sections [0094] to [0099]).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made, in view of Di Luzio et al and Yvin et al., to have used the method of Di Luzio et al. to prepare a composition comprising a combination of a antineoplastic agent such as cyclophosphamide and laminarin to treat cancer (tumors), since the combination of compounds that are used to treat the same diseases or conditions are well known in the art. More

specifically, it is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose. In re Kerkhoven, 626 F.2d 846, 205 U.S.P.Q. 1069 (C.C.P.A. 1980).

One having ordinary skill in the art would have been motivated in view of Di Luzio et al and Yvin et al., to have used the method of Di Luzio et al. to prepare a composition comprising a combination of an antineoplastic agent such as cyclophosphamide and laminarin to treat cancer (tumors), because a skilled artisan would reasonably be expected to prepare a composition comprising a combination of the compounds taught by Di Luzio et al and Yvin et al., to treat cancer (tumors) based on type, stage and/or severity of the cancer (tumors). It should be noted that the use of specific routes and ways of administration of said composition is common and obvious in the art, and is well within the purview of a skilled artisan.

Response to Amendment

Applicant's arguments filed 03/28/06 have been fully considered but they are not persuasive.

The applicant argues that the use of laminarin is novel and unobvious over DiLuzio who discloses and that laminarin is not identified in Di Luzio. However, 103 rejections to applicant's method are based on a combination of references (i.e, DiLuzio et al. in combination with Yvin et al). Furthermore, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The applicant argues that the Yvin et al. reference merely discloses the effects of soluble laminarin on tumor growth and that the cited Yvin et al. reference shows the superiority of laminarin in the particular field of tumor growth only with respect to the yeast derived glucan BEI used for comparison, as appears from paragraph (0034). However, Yvin et al. disclose that an object of the invention is the treatment of tumors and more generally of cancers by administering an effective amount of laminarin to a patient (see page 4, section [0099]).

The applicant argues that Yvin et al. would not suggest the regenerating activity of laminarin. However, the regenerating activity of laminarin is considered an inherent effect of the laminarin and does not appear alter the treatment of cancer by the said combination of laminarin and antineoplastic agent. As stated by applicant, the method of chemotherapeutic antineoplastic treatment according to the invention leads to a dramatic decrease of the well-known side effect which consists in the reduction of cells in the organism of a patient when administering antineoplastic agents (see page 13, lines 12-20 of applicant's specification). Thus the regenerating of cells by laminarin appears to decrease the side effect resulting from the administration of the antineoplastic agent.

The Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8.30am-5pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael C. Henry

7/28/06

Shaojia Anna Jiang, Ph.D.
Supervisory Patent Examiner
Art Unit 1623

July 27, 2006.